Accuracy of haemoglobin estimation by non-invasive Pulse Co-oximetry method: A prospective observational study among Neonates, Children and Young Adults

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Abstract

Background: At present, laboratory estimation of haemoglobin requires withdrawing of blood; a quick non-invasive technique without the requirement of blood sampling could be an ideal alternative provided it can consistently generate accurate values in the different subsets of the population. Aims & Objectives: The aim of this study was to evaluate the accuracy of non-invasive pulse co-oximetry based haemoglobin estimation (SpHb) in comparison with invasive laboratory-based haemoglobin values (IHb) with an objective to find out the feasibility of applying non-invasive Pulse Co-oximetry method for bed side haemoglobinometry. Study Design: This was a prospective, comparative and observational study; each subject when having their Hb estimated by auto-analyzer acted as a control in a cross over manner. Setting: This study was conducted in various clinical settings of K P C Medical College & Hospital, Jadavpur, Kolkata. Materials and Methods: Two hundred and twenty-five haemodynamically stable patients of different age groups from both sexes, divided into 3 equal groups of 75 patients each (Group 1 – neonatal population, Group 2 – patients around 10 years of age and Group 3 – patients around 20 years of age) were included to complete this study in a cross-over manner. Statistics: Data were tabulated in the computer and were later analyzed with statistical Student’s t-test and Chi-Square test for parametric data and categorical data, respectively. P value of <0.05 was taken as significant.

Results: Neonatal mean SpHb was insignificantly higher (p = 0.90) than the IHb (14.39 ± 1.23 g/dl vs. 14.38 ± 1.05 g/dl); whereas, mean SpHb values were insignificantly lower than that of IHb in both the groups having ages around 10 years (p=0.28; [11.25± 0.67 g/dl vs.11.30 ± 0.78 g/dl] and around 20 years (p=0.49; [12.89 ±1.7 g/dl vs.12.93 ± 1.78 g/dl]). Conclusions: Therefore, our study demonstrates that non-invasive pulse co-oximetry based haemoglobin estimation method (SpHb) is feasible in clinical setup and can generate comparable values to that of invasive laboratory-based auto-analyzer method of haemoglobin estimation (IHb) in a population of neonates to young adults.

Keywords: Pulse Co-oximetry, Non-invasive, Haemoglobin estimation.

INTRODUCTION

Haemoglobin (Hb) concentration and oxygen saturation are indicative of a patient’s ability to transport oxygen, thus, requiring its monitoring in any instance where oxygen transport is thought to be compromised [1]. In a hospital set up, patients undergo treatment in its various locations such as Out Patient Department (OPD), Casualty, Operation Theater (OT), Intensive Care Unit (ICU), Neonatal Intensive Care Unit (NICU) etc. and require frequent and often quick estimations of Hb values for proper management of their illness including trigger induced blood transfusion to avoid/reduce hazards of complications associated with transfusion therapy [2, 3]. Commonly, invasive methods (requiring samples of blood from arterial, venous or capillary sources) namely, auto-analyzers based estimations or Hemocue devices are used for Hb estimation with their associated actual as well as potential drawbacks such as consumption of valuable time (especially in emergency), phlebotomy-induced anaemia, pain, infection, and more involvement of human resources for processing of blood, equipments and reporting of measured values [4, 5].

Recently developed Pulse Co-Oximetry technique (Masimo Inc. CA, USA) allows not only non-invasive Hb estimation (without necessitating sampling of blood), but also provides a real-time continuous measurement of Hb concentration [6]. The observation of the ‘trend’ of haemoglobin could prove to be of immense clinical value with regard to decision making regarding blood transfusion.

This method is now under investigation throughout the globe and studies involving adult populations have
produced variable results ranging from strong correlation to sub-optimal estimation of Hb values as compared to laboratory methods\textsuperscript{17-11}. Evidence of its application in children and neonatal population is still limited. One study involving premature babies of less than 32 weeks gestational period shows a good correlation of pulse oximetry based estimation to that of standard laboratory values\textsuperscript{[11]}. From these studies, it appears that the application of this technique has immense potential in new born population as well as in children who often require multiple phlebotomies for frequent Hb estimation in a hospital set up.

On the basis of this little or variable evidence, we had conducted this prospective observational study to find out the feasibility and accuracy of non-invasive Pulse Co-Oximetry based Hb estimation among the population of various age groups, in a cross-over comparative manner, with invasive laboratory-based Hb estimation.

**MATERIAL & METHODS**

Following approval of Institutional Ethics Committee (No-KPCMCH /IEC/ 312 dated 17/12/2015) and after obtaining informed consent from candidates or their guardians, 225 hemodynamically stable patients of either sex were included in this prospective cross over based comparative study at our institute. Subjects were patients either admitted or visiting different OPDs of this institution viz. Gynecology & Obstetrics ward, Labor Room, OT, Post-natal ward, Paediatrics ward, Medicine ward, OPD & Casualty. They were divided into three subsets of population based on their range of age: Group 1 had patients comprising of neonates, Group 2 had patients in the age group of around 10 years and Group 3 included patients who were around 20 years of age. Patients who had known haemoglobinopathies, chronic kidney disease, infection, trauma or burn contracture of fingers, vasculitis, peripheral vascular disease, congenital heart disease, left to right shunt disorders and co-arctation of aorta were excluded from this study. Babies who had sub-optimal APGAR score were also excluded from this study.

First, each patient’s haemoglobin was measured by pulse co-oximetry. The pulse co-oximetry probe (Radical-7, Masimo Inc. Irvine, CA, USA) was placed on the ring finger of the left hand and the display monitor was noted for the appearance of the pulse co-oximetry tracing, pulsatility index (PI), SpO\textsubscript{2} value and the estimated Hb value. Values of each parameter after 2 minutes of continuous measurement were noted to get a steady and consistent result. The reusable pulse co-oximetry probe had two parts: one part being attached to the monitor, while the other part being attached to the finger probe. Both the parts were joined together in a detachable fashion at the centre of the cable. After removing the probe from the finger of one subject and before applying it to another subject, the two parts of the cable were first disconnected and then reconnected again. This was done to erase the memory of the previous reading (cache memory) so as to obtain each result without any confounding factor. Other parameters which had been noted for analysis included age, sex, body weight/birth weight, the age of parents (in case of neonate), SpHb and invasive Hb (IHb).

Next, each patient’s laboratory value (Autoanalyzer - Shenzhen Mindray Bio-Medical Electronics Co. Ltd, BC- 5380, PRC) of Hb that was done within last two days was collected. The Hb values obtained in the hospital laboratory more than two days back were not included in the study; in this case, fresh haemoglobin estimation was done in the laboratory of our institution and the values were collected accordingly. After completion of the study, the data were analyzed with statistical tools and SPSS software. Student’s t-test was applied for comparison of parametric variables and Chi-Square test was used for analysis of categorical data using IBM SPSS Amos Version 23.0 for Windows (Armonk, NY: IBM Corp). A calculated P value of < 0.05 was taken as significant.

**STATISTICAL ANALYSIS**

There were 75 patients in each group for this study. The data were manually collected, compiled and tabulated in the computer in Microsoft Excel. After completion of the study, this data was analyzed with statistical tools and SPSS software. Student’s t-test as well as Chi-Square test were applied accordingly, based on the parametric or categorical nature of the variables, using IBM SPSS Amos Version 23.0 for Windows (Armonk, NY: IBM Corp). Calculated P value of < 0.05 was taken as significant.

**RESULTS**

Table-1 depicts demographic and other parameters of the 3 study groups in details. In Group 1, the mean age of the fathers and mothers were 30.29 ± 3.74 (years) and 24.21 ± 3.68 (years), respectively. Mean APGAR scores at 1 min and 5 min were 8.7 ± 0.7 and 9.4 ± 0.6, respectively. The sex ratios of subjects in Gr 1, Gr 2 and Gr 3 were 32:43 (M: F), 34:41 (M: F) and 29:46 (M: F), respectively.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>GROUP 1 (n = 75)</th>
<th>GROUP 2 (n = 75)</th>
<th>GROUP 3 (n = 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days/years)</td>
<td>2.12±0.32</td>
<td>10.78±0.85</td>
<td>19.76±0.89</td>
</tr>
<tr>
<td>(mean ± SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length/Height(cm)</td>
<td>46.74±4.09</td>
<td>121.98±6.20</td>
<td>150.6±5.93</td>
</tr>
<tr>
<td>(mean ±SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>2.12±0.32</td>
<td>30.08±2.25</td>
<td>48.05±4.57</td>
</tr>
<tr>
<td>(meantSD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>139.52±3.86</td>
<td>88.48±2.88</td>
<td>88.84±4.58</td>
</tr>
<tr>
<td>(meantSD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulsatility Index (PI)</td>
<td>2.03±0.28</td>
<td>2.07±0.25</td>
<td>2.12±0.36</td>
</tr>
<tr>
<td>(meantSD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SpO2 (%)</td>
<td>95.93±10.22</td>
<td>97.88±0.89</td>
<td>97.61±0.92</td>
</tr>
<tr>
<td>(meantSD)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The mean SpHb and IHb values of 75 neonates in Gr 1 were 14.39 ± 1.23 (g/dl) and 14.38 ± 1.05 (g/dl) respectively (Table-2). The difference between these two mean values was not statistically significant (P = 0.90). The mean SpHb and IHb values of 75 subjects in Gr 2 were 11.25 ± 0.67 (g/dl) and 11.30 ± 0.78 (g/dl) respectively (Table-3). The difference between these two mean values was not statistically significant (P = 0.49).

Table 2: Comparison of non-invasive, pulse co-oximetry haemoglobin (SpHb) and invasive, laboratory auto-analyzer haemoglobin (IHb) values (g%) among the subjects of neonatal group (Gr-1)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean SpHb±SD</th>
<th>Mean IHb±SD</th>
<th>Paired Difference of Mean Hb</th>
<th>95% Confidence interval of the Mean Paired Difference of Mean Hb</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14.39±1.23</td>
<td>14.38±1.05</td>
<td>0.008</td>
<td>0.564</td>
<td>0.90</td>
</tr>
</tbody>
</table>

In intra-group analysis, in Gr 1, the Hb values obtained by pulse co-oximetry were marginally higher than that of the laboratory auto-analyzer values, whereas, the Hb values obtained by pulse co-oximetry in Gr 2 and Gr 3 were marginally lower than that of the laboratory Hb values (p = 0.90, 0.28 and 0.49, respectively). (Table-2,3 & 4). Accordingly, percentage deviation of mean values of Hb obtained by pulse co-oximetry method from those of laboratory method was 0.07%, 0.44% and 0.31% respectively, in Gr1, Gr 2 and Gr 3. (Table-5) In other words, the mean difference of Hb values obtained by pulse co-oximetry and laboratory auto-analyzer methods were 0.01 g/dl, 0.05 g/dl and 0.04 g/dl respectively, in Gr 1, Gr 2 and Gr 3. (Table-5)

Table 3: Comparison of non-invasive, pulse co-oximetry haemoglobin (SpHb) and invasive, laboratory auto-analyzer haemoglobin (IHb) values (g%) among the subjects of age group around 10 years (Gr-2)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean SpHb±SD</th>
<th>Mean IHb±SD</th>
<th>Paired Difference of Mean Hb</th>
<th>95% Confidence interval of the Mean Paired Difference of Mean Hb</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11.25±0.67</td>
<td>11.30±0.78</td>
<td>0.05</td>
<td>0.43</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Table 4: Comparison of non-invasive, pulse co-oximetry haemoglobin (SpHb) and invasive, laboratory auto-analyzer haemoglobin (IHb) values (g%) among the subjects of age group around 20 years (Gr-3)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean SpHb±SD</th>
<th>Mean IHb±SD</th>
<th>Paired Difference of Mean Hb</th>
<th>95% Confidence interval of the Mean Paired Difference of Mean Hb</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12.89±1.70</td>
<td>12.93±1.78</td>
<td>0.03</td>
<td>0.45</td>
<td>0.49</td>
</tr>
</tbody>
</table>

Table 5: Intra-group deviation of SpHb in values in terms of % or g/dl as compared to invasive Hb values

<table>
<thead>
<tr>
<th>Gr</th>
<th>Parameters</th>
<th>Mean difference of Hb (%)</th>
<th>Mean difference of Hb (g/dl)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14.39±1.23: 14.38±1.05</td>
<td>0.07</td>
<td>0.01</td>
<td>0.90</td>
</tr>
<tr>
<td>2</td>
<td>11.25±0.67: 11.30±0.78</td>
<td>0.44</td>
<td>0.05</td>
<td>0.28</td>
</tr>
<tr>
<td>3</td>
<td>12.89±1.70: 12.93±1.78</td>
<td>0.31</td>
<td>0.04</td>
<td>0.49</td>
</tr>
</tbody>
</table>

DISCUSSION:

**General Discussion:**

Our study compared the accuracy of the haemoglobin values estimated by Pulse co-oximetry technique to the haemoglobin values estimated by the laboratory auto-analyzer in a cohort of 225 patients of different age groups.

The difference between the mean values of haemoglobin measured by pulse co-oximetry among neonates in Gr 1 (14.39±1.23) was comparable to the haemoglobin values obtained in this group by laboratory auto-analyzer (14.38±1.05) method. The intra-group percentage difference of haemoglobin between the two methods was 0.07%. Similarly, there was insignificant difference between the mean values of haemoglobin obtained by pulse co-oximetry (11.25±0.67) and auto-analyzer (11.30±0.78) methods among the population aged around 10 years in Gr 2. The intra-group difference of measured Hb by two methods was 0.44%. We also found that the mean haemoglobin values obtained by pulse co-oximetry (12.89±1.70) and laboratory auto-analyzer (12.93±1.78) methods were also comparable in group 3 (patients having their ages around 20 years). The percentage difference between the two values was 0.31%.

As per the ‘Clinical Laboratories Improvement Act’, a maximum of 7% deviation of the measured Haemoglobin level from the expected value can be clinically accepted [12]. This corresponds to a deviation of about 1g/dl. Any deviation beyond this is considered to be incorrect measurement. Therefore, our study shows that in haemodynamically stable subjects, Pulse co-oximetry can accurately measure haemoglobin values as compared to the laboratory auto-analyzer.

As per ‘The International Committee for Standardization in Haematology Reference Method’, the Cyanmethaemoglobin (HiCN)
method is the ‘Gold standard’ for estimation of haemoglobin. This is often not practical for routine clinical use, thus, paving the way for the laboratory auto-analyzer to become the next best option for the invasive method of haemoglobin estimation [10]. However, estimation of haemoglobin in the laboratory by auto-analyzer is also not without bias. Investigations have shown that the laboratory auto-analyzer value of haemoglobin also may deviate within a range of 0.1 mg to 0.5 g/dl when compared to HiCN method [13].

In our study, we have got deviations of 0.07%, 0.44% and 0.31%, (0.01g/dl, 0.05 g/dl and 0.04 g/dl) in mean haemoglobin values measured by pulse co-oximetry method when compared to those of auto-analyzer method respectively, in Group 1, 2 and 3. This degree of deviation is well within the prescribed limits as per the Clinical Laboratories Improvement Act [12]. So, we can infer that the deviations of Hb values we got by using pulse co-oximetry method are well within acceptable range.

**Discussion of Relevant Studies Involving Adult Population:**

In 2007, Macknet MR et al published their first preliminary study comparing the accuracy of pulse co-oximetry based haemoglobin estimation, in an ‘abstract’ form [14]. Later on, in 2010, they published the results of a full study involving 20 healthy volunteers that showed good correlation between pulse co-oximetry and laboratory auto-analyzer based haemoglobin values [15].

Frasca D et al, in 2011, in their study involving 62 patients in the ICU, found that SpHb had absolute accuracy not only in spot-values of haemoglobin but also in the monitoring of ‘trend’ of haemoglobin values [16]. In this study, a few patients had a deviation of up to 1 g/dl between the two methods; however, overall, there was a strong correlation between the techniques for measuring Hb. In our study, the adult patients, (group 3) had lower haemoglobin values (downward deviation) compared to laboratory values. However, these deviations were statistically insignificant and pulse co-oximetry haemoglobin values had an absolute correlation with laboratory auto-analyzer values. Thus, our results were similar to results obtained by Frasca D et al in their study.

In the year 2011, Causey MW et al conducted another study involving surgical and ICU patients requiring haemodynamic monitoring [17]. Their study found a mean difference of 0.5 g/dl in the haemoglobin values measured by the two methods. This difference was statistically insignificant and the pulse co-oximetry based haemoglobin values had good correlation with the laboratory-based haemoglobin values. In our study too, the mean difference of haemoglobin values measured by the two methods, among the adult patients (group 3) was 0.04 g/dl. Similar to the results obtained by Causey MW et al, our study also found a good correlation between the two methods of measurement. Moreover, compared to Causey et al, we obtained a lesser difference in mean haemoglobin values (0.04 g/dl versus 0.5 g/dl) which can be attributed to the inclusion of non-ICU and non-surgical healthy, adult patients in our study, having better haemodynamic stability.

In 2012, Coquin J et al, however, found a negative correlation between the haemoglobin values obtained by the pulse co-oximeter and the laboratory auto-analyzer [18]. Their study involved 33 haemodynamically unstable patients admitted to the ICU with severe gastrointestinal bleed. These patients had very poor pulsatility index in plethysmograph resulting in yielding of incorrect or un-recordable SpHb values. Unlike their study population, the patient population in our study was haemodynamically stable, with no history of any bleeding, with stable pulsatility index, signifying good capability of pulse co-oximetry based haemoglobin estimation. Raikel M, in 2012, conducted a study involving 155 patients from the OPD, which showed a good correlation and accuracy of pulse co-oximetry compared to the laboratory method of haemoglobin estimation [19]. Like his study, our study also involved haemodynamically stable patient population producing similar results.

In 2014, Saito J et al, in their study, while inducing acute normovolemic haemodilution and subsequent autologous blood transfusion, found a marginal negative correlation between the haemoglobin measurements by pulse co-oximetry and laboratory methods [20]. The mean deviation of haemoglobin in their study varied between 1.10 to 1.43 g/dl. As per Clinical Laboratories Improvement Act of guidelines, a deviation of > 1g/dl between two methods is clinically significant, thereby, implicating a tendency of higher values of haemoglobin by pulse co-oximetry. Compared to their study, our study did not have any such significant deviation although patients in group 1 had clinically and statistically insignificant higher values of haemoglobin estimation by pulse co-oximetry method. In Saito’s study, there occurred rapid changes in haemoglobin concentration because of induced acute normovolemic haemodilution followed by autologous blood transfusion, thereby, creating a rapid shift in the optical characteristics of blood components. Pulse co-oximetry based haemoglobin estimation depends on wavelength based spectrophotometry and because of rapid shifting of optical characteristics of blood, the negative correlation in the results might have occurred. Our patient population had stable haemodynamics with no history of recent blood transfusion or bleeding, thereby, providing a positive correlation in results between the two methods of measurement.

**Discussion of Relevant Studies Involving Paediatric Population:**

In 2013, Amano I et al conducted a study involving 110 children (3-year-olds) for anaemia screening using pulse co-oximetry while comparing its values with laboratory methods [21]. They had found a good correlation between the two methods. Our study had also included a subset of the paediatric population (group 2) and we too have found similar results. Our study population as well as that of Amano I et al was stable haemodynamically, which have probably contributed to similar results.

In 2016, Ryan ML et al evaluated the accuracy of non-invasive haemoglobin monitoring by pulse co-oximetry in paediatric trauma patients compared to both l-stat device as well as the laboratory auto-analyzer [22]. Their study involved 114 patients aged less than 17 years. As compared to l-stat, SpHb had a mean difference of lower value by 0.39 g/dl and when compared to the laboratory auto-analyzer, SpHb values were lower by 0.49 g/dl; the difference being well within the acceptable limits of deviation between two methods as per the Clinical Laboratories Improvement Act [23]. In the paediatric population in our study, SpHb values of patients of group 2 were lower by 0.05 g/dl compared to the laboratory auto-analyzer values, suggesting a good correlation between the two methods. Thus, results of our study in this subset of the population were similar to those obtained by Ryan et al. In another recent study (2017) involving children, Lewy TS et al found that the pulse co-oximeter underestimated the haemoglobin values compared to laboratory method by 1.62 g/dl (i.e. more than the accepted limit of deviation between two methods as per CLIA) [13, 24]. Unlike our study, their patient population involved a more young group of paediatric population (1-5-year-olds), which might have contributed to the variation in the results.

**Discussion of Relevant Studies Involving Patients of Neonatal Age Group:**

A study by Jung YH et al, in 2013, involving 56 term and preterm neonates, showed a good correlation between the haemoglobin values obtained by pulse co-oximetry and laboratory method with an insignificant upward deviation of the SpHb values. Our study had also shown an insignificant upward deviation of SpHb values in neonates (group 1), similar to their study.
Recently, in 2015, Nicholas C et al, in their study involving neonates including preterm, had found a moderate degree of positive correlation between the two methods of haemoglobin estimation [11]. Results of our study, in group 1 involving only term neonates, had shown a strong correlation between SpHb and laboratory auto-analyzer methods. Unlike this study, the higher degree of correlation in our study might have been because of better circulatory status in the neonates of our study population which did not include the preterm neonates.

Very recently, in 2017, Garcia-Soler P et al evaluated the validity of pulse co-oximetry among 80 critically ill neonates with a haemorrhagic potential [22]. Despite critical illness and bleeding tendency, they found a good over-all correlation between the haemoglobin measurements by the two methods. The strong correlation of values in our study could be due to the inclusion of only healthy neonates with better circulatory status.

Unlike all the previously mentioned studies, our study is unique in nature because of inclusion of patient population from different age groups. Till now, most of the studies done have used either adult or neonatal subjects; very few studies have included patients from all age groups. However, results of our study, when compared to other previous studies, reveal that pulse co-oximetry based haemoglobin estimation can provide a reliable estimation of haemoglobin values compared to the invasive auto-analyzer technology. Unlike our study, many studies conducted in subsets of the population with a clinical situation of poor circulatory state or bleeding tendency, have generated mostly negative correlation in the haemoglobin values obtained by the two methods. Results of our study have differed from such studies with negative correlation. The reason for the good correlation in our study might be because of the low-risk category of our patients, as far as the circulatory status is concerned.

CONCLUSION

Recent studies across the globe reveal good correlation of haemoglobin values obtained by pulse co-oximetry method of estimation in comparison to invasive methods among haemodynamically stable patients; moderately good correlation in paediatric and neonatal population, and to some extent unpredictable results in haemodynamically unstable patients with active bleeding. Our study population had included haemodynamically stable patients with strict exclusion criteria, revealing results comparable to results of those studies conducted among haemodynamically stable patients in various other centres. Thus, it may be concluded that non-invasive pulse co-oximetry based haemoglobin estimation can generate comparable values to that of invasive laboratory-based auto-analyzer method in a population of neonates to young adults. Our study also emphasizes that pulse co-oximetry based haemoglobin estimation can be a feasible alternative to the invasive method in the hospital set-up, thus, avoiding frequent venepuncture and its consequent risks and sequelae.

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REFERENCES